

PCT

WORLD INTELLECTUAL PROPERTY ORGANIZATION  
International Bureau



D12

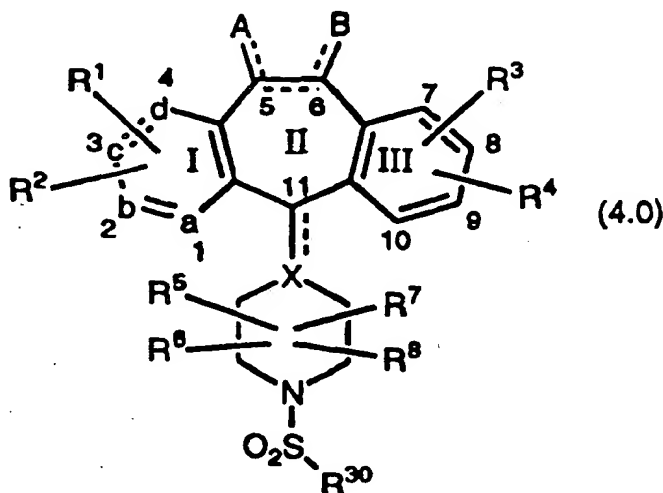
INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

<p>(51) International Patent Classification <sup>6</sup> : C07D 401/04, A61K 31/445, C07D 221/16, 401/14</p>	<p>A1</p>	<p>(11) International Publication Number: WO 95/10514 (43) International Publication Date: 20 April 1995 (20.04.95)</p>
<p>(21) International Application Number: PCT/US94/11390 (22) International Filing Date: 12 October 1994 (12.10.94) (30) Priority Data: 08/137,856 15 October 1993 (15.10.93) US (71) Applicant: SCHERING CORPORATION [US/US]; 2000 Galloping Hill Road, Kenilworth, NJ 07033 (US). (72) Inventors: BISHOP, W., Robert; 17 Hopper Avenue, Pompton Plains, NJ 07444 (US). DOLL, Ronald, J.; 126 Union Avenue, Maplewood, NJ 07040 (US). MALLAMS, Alan, K.; 147 Kings Highway, Hackettstown, NJ 07840 (US). NJORGE, F., George; 2597 Juliat Place, Union, NJ 07083 (US). PETRIN, Joanne, M.; 27 Anderson Parkway, Cedar Grove, NJ 07009 (US). PIWINSKI, John, J.; 6 Saddle Ridge Drive, Lebanon, NJ 08833 (US). (74) Agent: JEANETTE, Henry, C.; Schering-Plough Corporation, Patent Dept. K-6-1 1990, 2000 Galloping Hill Road, Kenilworth, NJ 07033-0530 (US).</p>	<p>(81) Designated States: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, JP, KG, KR, KZ, LK, LR, LT, LV, MD, MG, MN, NO, NZ, PL, RO, RU, SI, SK, TJ, TT, UA, UZ, VN, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG), ARIPO patent (KE, MW, SD, SZ).  Published With international search report.</p>	

(54) Title: TRICYCLIC SULFONAMIDE COMPOUNDS USEFUL FOR INHIBITION OF G-PROTEIN FUNCTION AND FOR TREATMENT OF PROLIFERATIVE DISEASES

(57) Abstract

A method of inhibiting Ras function and therefore inhibiting cellular growth is disclosed. The method comprises the administration of a compound containing a tricyclic ring system to a biological system. In particular, the method inhibits cellular growth in a mammal such as a human being. Novel compounds of formula (4.0) are disclosed. Also disclosed are processes for making 3-substituted compounds of formula (4.0). Further disclosed are novel compounds which are intermediates in the processes for making the 3-substituted compounds of formula (4.0).



# PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>71 125 a/ea</b>	<b>FOR FURTHER ACTION</b> see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. <b>PCT/EP 97/03245</b>	International filing date (day/month/year) <b>20/06/1997</b>	(Earliest) Priority Date (day/month/year) <b>20/06/1996</b>
Applicant <b>KLINGE PHARMA GMBH et al.</b>		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. ☒ Certain claims were found unsearchable (see Box I).

2. ☐ Unity of invention is lacking (see Box II).

3. ☐ The international application contains disclosure of a nucleotide and/or amino acid sequence listing and the international search was carried out on the basis of the sequence listing

☐ filed with the international application.

☐ furnished by the applicant separately from the international application,

☐ but not accompanied by a statement to the effect that it did not include matter going beyond the disclosure in the international application as filed.

☐ Transcribed by this Authority

4. With regard to the title, ☐ the text is approved as submitted by the applicant.

☒ the text has been established by this Authority to read as follows:

**PYRIDYL ALKENE- AND PYRIDYL ALKINE- ACID AMIDES AS CYTOSTATICS AND IMMUNOSUPPRESSIVES.**

5. With regard to the abstract,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this International Search Report, submit comments to this Authority.

6. The figure of the drawings to be published with the abstract is:

Figure No. - ☐ as suggested by the applicant.

☐ None of the figures.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

## INTERNATIONAL SEARCH REPORT

International application No.  
PCT/EP 97/03245**Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)**

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claims Nos.: 1-8, 17  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  
The subject-matter of the present claims 1-8, 17 is so broad that a complete search is not possible on economic grounds (PCT Search Guidelines III, 3.6 and 3.7). Therefore the search has been based on the examples and the other claims.
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

**Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)**

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

## INTERNATIONAL SEARCH REPORT

International Application No  
PCT/EP 97/03245

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 C07D401/12 C07D405/14 C07D409/14 A61K31/44

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 C07D A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 330 026 A (TAKEDA CHEMICAL INDUSTRIES LTD) 30 August 1989 cited in the application see table 1	1-40
A	--- EP 0 343 307 A (ESPANOLA PROD QUIMICOS) 29 November 1989 see the whole document -----	1-40

☐ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

## \* Special categories of cited documents :

\*A\* document defining the general state of the art which is not considered to be of particular relevance

\*E\* earlier document but published on or after the international filing date

\*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

\*O\* document referring to an oral disclosure, use, exhibition or other means

\*P\* document published prior to the international filing date but later than the priority date claimed

\*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

\*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

\*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

\*&amp;\* document member of the same patent family

Date of the actual completion of the international search

23 September 1997

Date of mailing of the international search report

3 0. 09. 97

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+ 31-70) 340-2040, Tx. 31 651 epo nl,  
Fax (+ 31-70) 340-3016

Authorized officer

Bosma, P

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 97/03245

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0330026 A	30-08-89	AT 112560 T DE 68918609 D DE 68918609 T JP 2138255 A US 5169856 A	15-10-94 10-11-94 04-05-95 28-05-90 08-12-92
EP 0343307 A	29-11-89	NONE	

PCT

WORLD INTELLECTUAL PROPERTY ORGANIZATION  
International Bureau

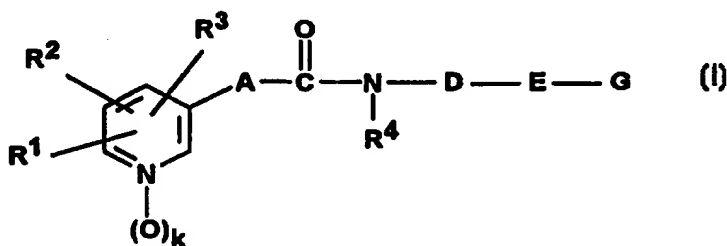
## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification <sup>6</sup> : <b>C07D 401/12, 405/14, 409/14, A61K 31/44</b>		A1	(11) International Publication Number: <b>WO 97/48696</b>
			(43) International Publication Date: 24 December 1997 (24.12.97)
(21) International Application Number: PCT/EP97/03245		(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG).	
(22) International Filing Date: 20 June 1997 (20.06.97)			
(30) Priority Data: 196 24 659.8 20 June 1996 (20.06.96)			
(71) Applicant (for all designated States except US): KLINGE PHARMA GMBH [DE/DE]; Berg-am-Laim-Strasse 129, D-81673 Munich (DE).			
(72) Inventors; and (75) Inventors/Applicants (for US only): BIEDERMANN, Elfi [DE/DE]; Zugspitzstrasse 93, D-85591 Vaterstetten (DE). ✓ HASMANN, Max [DE/DE]; Lerchenweg 9, D-82061 Neuried (DE). ✓ LÖSER, Roland [DE/DE]; Fichtenweg 2, D-82340 Feldafing (DE). ✓ RATTEL, Benno [DE/DE]; Eichelhäherstrasse 3, D-81249 Munich (DE). ✓ REITER, Friedemann [DE/DE]; Zugspitzstrasse 36, D-85640 Putzbrunn (DE). ✓ SCHEIN, Barbara [DE/DE]; Sudetenweg 4, D-85375 Neufahrn (DE). ✓ SEIBEL, Klaus [DE/DE]; Haberlstrasse 9, D-82166 Gräfelfing (DE). ✓ VOGT, Klaus [DE/DE]; Balanstrasse 63, D-81541 Munich (DE).		Published With international search report.	
(74) Agents: KOLB, Helga et al.; Hoffmann. Eitle, Arabellastrasse 4, D-81925 Munich (DE).			

(54) Title: PYRIDYL ALKENE- AND PYRIDYL ALKINE- ACID AMIDES AS CYTOSTATICS AND IMMUNOSUPPRESSIVES

## (57) Abstract

The invention relates to new pyridyl alkane and pyridyl alkine acid amides according to general formula (I), as well as methods for their production, medicaments containing these compounds as well as their medical use, especially in the treatment of tumors or for immunosuppression.



**FOR THE PURPOSES OF INFORMATION ONLY**

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
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AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
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CZ	Czech Republic	LC	Saint Lucia	RU	Russian Federation		
DE	Germany	LI	Liechtenstein	SD	Sudan		
DK	Denmark	LK	Sri Lanka	SE	Sweden		
EE	Estonia	LR	Liberia	SG	Singapore		

# INTERNATIONAL SEARCH REPORT

Inter. Application No  
PCT/EP 97/03245

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 C07D401/12 C07D405/14 C07D409/14 A61K31/44

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 C07D A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 330 026 A (TAKEDA CHEMICAL INDUSTRIES LTD) 30 August 1989 cited in the application see table 1	1-40
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☐ Further documents are listed in the continuation of box C.

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### \* Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*Z\* document member of the same patent family

Date of the actual completion of the international search

23 September 1997

Date of mailing of the international search report

3 0. 09. 97

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+ 31-70) 340-2040, Tx. 31 651 epo nl,  
Fax (+ 31-70) 340-3016

Authorized officer

Bosma, P



# INTERNATIONAL SEARCH REPORT

International application No.

PCT/EP 97/03245

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claims Nos.: 1-8, 17  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:  
The subject-matter of the present claims 1-8, 17 is so broad that a complete search is not possible on economic grounds (PCT Search Guidelines III, 3.6 and 3.7). Therefore the search has been based on the examples and the other claims.
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 97/03245

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0330026 A	30-08-89	AT 112560 T DE 68918609 D DE 68918609 T JP 2138255 A US 5169856 A	15-10-94 10-11-94 04-05-95 28-05-90 08-12-92
EP 0343307 A	29-11-89	NONE	

PATENT COOPERATION TREATY

Bitte ablegen  
(Austskil)

From the INTERNATIONAL BUREAU

PCT

NOTIFICATION OF RECEIPT OF  
RECORD COPY

(PCT Rule 24.2(a))

To:

KOLB, Helga  
Hoffmann, Eitle  
Arabellastrasse 4  
D-81925 Munich  
ALLEMAGNE

EINGEGANGEN

21. Juli 1997

HOFFMANN - EITLE, MÜNCHEN  
PATENTANWÄLTE RECHTSANWÄLTE

Date of mailing (day/month/year) 15 July 1997 (15.07.97)	IMPORTANT NOTIFICATION
Applicant's or agent's file reference 71 125 a/ea	International application No. PCT/EP97/03245

The applicant is hereby notified that the International Bureau has received the record copy of the international application as detailed below.

Name(s) of the applicant(s) and State(s) for which they are applicants:

KLINGE PHARMA GMBH (for all designated States except US)  
BIEDERMANN, Elfi et al (for US).

International filing date : 20 June 1997 (20.06.97)

Priority date(s) claimed : 20 June 1996 (20.06.96)

Date of receipt of the record copy  
by the International Bureau : 15 July 1997 (15.07.97)

List of designated Offices :

AP : GH, KE, LS, MW, SD, SZ, UG, ZW

EA : AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

EP : AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

OA : BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

National : AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU,  
IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU,  
SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW

## ATTENTION

The applicant should carefully check the data appearing in this Notification. In case of any discrepancy between these data and the indications in the international application, the applicant should immediately inform the International Bureau.

In addition, the applicant's attention is drawn to the information contained in the Annex, relating to:

☒ time limits for entry into the national phase;

☐ confirmation of precautionary designations;

☐ requirements regarding priority documents.

A copy of this Notification is being sent to the receiving Office and to the International Searching Authority.

The International Bureau of WIPO  
34, chemin des Colombettes  
1211 Geneva 20, Switzerland

Authorized officer:

Marie-José Devillard

Facsimile No. (41-22) 740.14.35

Telephone No. (41-22) 338.83.38

## INFORMATION ON TIME LIMITS FOR ENTERING THE NATIONAL PHASE

The applicant is reminded that the "national phase" must be entered before each of the designated Offices indicated in the Notification of Receipt of Record Copy (Form PCT/IB/301) by paying national fees and furnishing translations, as prescribed by the applicable national laws.

The time limit for performing these procedural acts is **20 MONTHS** from the priority date or, for those designated States which the applicant elects in a demand for international preliminary examination or in a later election, **30 MONTHS** from the priority date, provided that the election is made before the expiry of 19 months from the priority date. Some designated (or elected) Offices have fixed time limits which expire even later than 20 or 30 months from the priority date. In other Offices an extension of time or grace period, in some cases upon payment of an additional fee, is available.

In addition to these procedural acts, the applicant may also have to comply with other special requirements applicable in certain Offices. It is the applicant's responsibility to ensure that the necessary steps to enter the national phase are taken in a timely fashion. Most designated Offices do not issue reminders to applicants in connection with the entry into the national phase.

For detailed information about the procedural acts to be performed to enter the national phase before each designated Office, the applicable time limits and possible extensions of time or grace periods, and any other requirements, see the relevant Chapters of Volume II of the PCT Applicant's Guide. Information about the requirements for filing a demand for international preliminary examination is set out in Chapter IX of Volume I of the PCT Applicant's Guide.

Note that since ES is not bound by PCT Chapter II (which provides for the international preliminary examination procedure), that State cannot be elected in a demand for international preliminary examination. In the case of the designation of ES for a national patent, the applicant must thus always enter the national phase before the national Office of that State before the expiration of 20 months from the priority date. In the case of the designation of ES for a European patent, however, the 31-month time limit applies in respect of that designation if at least one other State designated for a European patent is also elected within the 19-month period.\*

Note also that only an applicant who is a national or resident of a PCT Contracting State which is bound by Chapter II has the right to file a demand for international preliminary examination.

\* CH and LI became bound by PCT Chapter II on 1 September 1995. GR became bound by PCT Chapter II on 7 September 1996. Therefore, CH and LI may be elected in a demand or a later election filed on or after 1 September 1995, and GR may be elected in a demand or a later election filed on or after 7 September 1996, regardless of the filing date of the international application. (See 2nd paragraph above.)

## CONFIRMATION OF PRECAUTIONARY DESIGNATIONS

This notification lists only specific designations made under Rule 4.9(a) in the request. It is important to check that these designations are correct. Errors in designations can be corrected where precautionary designations have been made under Rule 4.9(b). The applicant is hereby reminded that any precautionary designations may be confirmed according to Rule 4.9(c) before the expiration of 15 months from the priority date. If it is not confirmed, it will automatically be regarded as withdrawn by the applicant. There will be no reminder and no invitation. Confirmation of a designation consists of the filing of a notice specifying the designated State concerned (with an indication of the kind of protection or treatment desired) and the payment of the designation and confirmation fees. Confirmation must reach the receiving Office within the 15-month time limit.

## REQUIREMENTS REGARDING PRIORITY DOCUMENTS

For applicants who have not yet complied with the requirements regarding priority documents the following is recalled.

Where the priority of an earlier national (i.e., national or regional) application is claimed, the applicant must submit a copy of the said national application, certified by the authority with which it was filed ("the priority document") to the receiving Office (which will transmit it to the International Bureau) or directly to the International Bureau, before the expiration of 16 months from the priority date (Rule 17.1).

Where the priority document is issued by the receiving Office, the applicant may, instead of submitting the priority document, request the receiving Office to prepare and transmit the priority document to the International Bureau. Such a request must be made before the expiration of the 16-month time limit.

It is recalled that, where several priorities are claimed, the priority date to be considered for the purposes of computing the 16-month time limit is the filing date of the earliest application whose priority is claimed.

If the priority document concerned is not submitted to the International Bureau before the expiration of the 16-month time limit, or if the request to the receiving Office to transmit the priority document has not been made (and the corresponding fee, if any, paid) before the expiration of this time limit, any designated State may disregard the priority claim.

## PATENT COOPERATION TREATY

Bille ablegen  
(Austskil)

From the INTERNATIONAL BUREAU

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(PCT Rule 24.2(a))

To:

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Hoffmann, Eitle  
Arabellastrasse 4  
D-81925 Munich  
ALLEMAGNE

EINGEGANGEN

21. Juli 1997

HOFFMANN · EITLE, MÜNCHEN  
PATENTANWÄLTE RECHTSANWÄLTE

Date of mailing (day/month/year) 15 July 1997 (15.07.97)	IMPORTANT NOTIFICATION
Applicant's or agent's file reference 71 125 a/ea	International application No. PCT/EP97/03245

The applicant is hereby notified that the International Bureau has received the record copy of the international application as detailed below.

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International filing date : 20 June 1997 (20.06.97)

Priority date(s) claimed : 20 June 1996 (20.06.96)

Date of receipt of the record copy  
by the International Bureau : 15 July 1997 (15.07.97)

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EP : AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

OA : BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

National : AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU,  
IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU,  
SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW

## ATTENTION

The applicant should carefully check the data appearing in this Notification. In case of any discrepancy between these data and the indications in the international application, the applicant should immediately inform the International Bureau.

In addition, the applicant's attention is drawn to the information contained in the Annex, relating to:

☒ time limits for entry into the national phase;

☐ confirmation of precautionary designations;

☐ requirements regarding priority documents.

A copy of this Notification is being sent to the receiving Office and to the International Searching Authority.

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Authorized officer: Marie-José Devillard
Facsimile No. (41-22) 740.14.35	Telephone No. (41-22) 338.83.38

## INFORMATION ON TIME LIMITS FOR ENTERING THE NATIONAL PHASE

The applicant is reminded that the "national phase" must be entered before each of the designated Offices indicated in the Notification of Receipt of Record Copy (Form PCT/IB/301) by paying national fees and furnishing translations, as prescribed by the applicable national laws.

The time limit for performing these procedural acts is **20 MONTHS** from the priority date or, for those designated States which the applicant elects in a demand for international preliminary examination or in a later election, **30 MONTHS** from the priority date, provided that the election is made before the expiry of 19 months from the priority date. Some designated (or elected) Offices have fixed time limits which expire even later than 20 or 30 months from the priority date. In other Offices an extension of time or grace period, in some cases upon payment of an additional fee, is available.

In addition to these procedural acts, the applicant may also have to comply with other special requirements applicable in certain Offices. It is the applicant's responsibility to ensure that the necessary steps to enter the national phase are taken in a timely fashion. Most designated Offices do not issue reminders to applicants in connection with the entry into the national phase.

For detailed information about the procedural acts to be performed to enter the national phase before each designated Office, the applicable time limits and possible extensions of time or grace periods, and any other requirements, see the relevant Chapters of Volume II of the PCT Applicant's Guide. Information about the requirements for filing a demand for international preliminary examination is set out in Chapter IX of Volume I of the PCT Applicant's Guide.

Note that since ES is not bound by PCT Chapter II (which provides for the international preliminary examination procedure), that State cannot be elected in a demand for international preliminary examination. In the case of the designation of ES for a national patent, the applicant must thus always enter the national phase before the national Office of that State before the expiration of 20 months from the priority date. In the case of the designation of ES for a European patent, however, the 31-month time limit applies in respect of that designation if at least one other State designated for a European patent is also elected within the 19-month period.\*

Note also that only an applicant who is a national or resident of a PCT Contracting State which is bound by Chapter II has the right to file a demand for international preliminary examination.

\* CH and LI became bound by PCT Chapter II on 1 September 1995. GR became bound by PCT Chapter II on 7 September 1996. Therefore, CH and LI may be elected in a demand or a later election filed on or after 1 September 1995, and GR may be elected in a demand or a later election filed on or after 7 September 1996, regardless of the filing date of the international application. (See 2nd paragraph above.)

## CONFIRMATION OF PRECAUTIONARY DESIGNATIONS

This notification lists only specific designations made under Rule 4.9(a) in the request. It is important to check that these designations are correct. Errors in designations can be corrected where precautionary designations have been made under Rule 4.9(b). The applicant is hereby reminded that any precautionary designations may be confirmed according to Rule 4.9(c) before the expiration of 15 months from the priority date. If it is not confirmed, it will automatically be regarded as withdrawn by the applicant. There will be no reminder and no invitation. Confirmation of a designation consists of the filing of a notice specifying the designated State concerned (with an indication of the kind of protection or treatment desired) and the payment of the designation and confirmation fees. Confirmation must reach the receiving Office within the 15-month time limit.

## REQUIREMENTS REGARDING PRIORITY DOCUMENTS

For applicants who have not yet complied with the requirements regarding priority documents the following is recalled.

Where the priority of an earlier national (i.e., national or regional) application is claimed, the applicant must submit a copy of the said national application, certified by the authority with which it was filed ("the priority document") to the receiving Office (which will transmit it to the International Bureau) or directly to the International Bureau, before the expiration of 16 months from the priority date (Rule 17.1).

Where the priority document is issued by the receiving Office, the applicant may, instead of submitting the priority document, request the receiving Office to prepare and transmit the priority document to the International Bureau. Such a request must be made before the expiration of the 16-month time limit.

It is recalled that, where several priorities are claimed, the priority date to be considered for the purposes of computing the 16-month time limit is the filing date of the earliest application whose priority is claimed.

If the priority document concerned is not submitted to the International Bureau before the expiration of the 16-month time limit, or if the request to the receiving Office to transmit the priority document has not been made (and the corresponding fee, if any, paid) before the expiration of this time limit, any designated State may disregard the priority claim.

# PATENT COOPERATION TREATY

REC'D	07 OCT 1998
WIPO	PCT

## PCT

### INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 71 125 a/se	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (PCT/IPEA/416)	
International application No. PCT/EP97/03245	International filing date (day/month/year) 20/06/1997	Priority date (day/month/year) 20/06/1996
International Patent Classification (IPC) or national classification and IPC C07D401/12		
Applicant KLINGE PHARMA GMBH et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.


2. This REPORT consists of a total of 5 sheets, including this cover sheet.

☒ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 1 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand 26/11/1997	Date of completion of this report 05. 10. 98
Name and mailing address of the IPEA/  European Patent Office D-80298 Munich Tel. (+49-89) 2399-0, Tx: 523656 epmu d Fax: (+49-89) 2399-4465	Authorized officer Von Daacke, A Telephone No. (+49-89) 2399-8286

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP97/03245

## I. Basis of the report

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

### Description, pages:

1-155 as originally filed

### Claims, No.:

1-40 as originally filed

41 as received on 31/07/1998 with letter of 31/07/1998

2. The amendments have resulted in the cancellation of:

- ☐ the description, pages:  
☐ the claims, Nos.:  
☐ the drawings, sheets:

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

## V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

### 1. Statement

Novelty (N)	Yes: Claims 1-41
	No: Claims
Inventive step (IS)	Yes: Claims 6-13,41
	No: Claims 1-5,14-40
Industrial applicability (IA)	Yes: Claims 1-41
	No: Claims



**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/EP97/03245

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**2. Citations and explanations**

**see separate sheet**

**VIII. Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

**see separate sheet**

## **SECTION V**

### **1. PRIOR ART**

The documents cited in the International Search Report

D1 = EP-A-0 330 026

D2 = EP-A-0 343 307

have been considered for the examination procedure.

### **2. NOVELTY**

The claimed subject-matter is considered to be novel. Compound 3 of D1 is excluded via a disclaimer at the end of Claim 1. D2 compounds do not include an alkenylene spacer 'A'. The D1 and D2 compounds are described as having CNS or H1 antagonistic activities (Article 33(2) PCT).

### **3. INVENTIVE STEP**

The subject-matter of Claims 1-5 and 14-40 does not fulfil the requirements of Art 33(3) PCT for the following reasons.

The application includes activity tests for seven compounds which are structurally very close together:  $R^1-R^4 = H$ ,  $k=0$ ,  $A = -CH=CH-$ ,  $D = \text{butylene}$ ,  $E = \text{piperidine-1,4-diyl}$ . Only G has different, but similar meanings. The Representative has filed additional experimental results and pharmaceutical tests which demonstrate that the structural unit D-E-G can be varied to a certain extent without any loss of the desired activity. For example, the unit 'G' may denote an aliphatic, aromatic or heteroaromatic system, wherein the aromatic ring is optionally substituted. The 'left' part of the molecule, i.e.  $R^1$ ,  $R^2$ ,  $R^3$ , and mostly  $R^4$ , as well still denote hydrogen in all of the tested compounds. Only table 1 which includes 'exemplary' compounds shows values other hydrogen for  $R^1$ . Even though it would be assumed that all of the exemplified compounds do actually exhibit the alleged activity what is not yet convincingly shown, only the object of Claims 6-13 can be regarded as inventive, i.e. solve the subjective problem for providing cytostatic and immunosuppressive agents. Any preceding claims include broad definitions

which cannot be regarded as a reasonable generalisation of the examples. In particular due to the definitions of R<sup>1</sup>-R<sup>4</sup> and possible substitutions of aromatic systems thereof (see at the end of the respective claims).

The process Claims 14-16 include preparation steps already known such that an Inventive step cannot per se be based thereupon.

Since Claims 18-40 relate to the pharmaceutical use (different categories) all of these claims do also not satisfy Art. 33(3) PCT.

Claim 17 covering the intermediate compounds with G=H does not fulfil the requirements of Art. 33(3) EPC, as well because it is referred back to Claims 1-7.

Between the present compounds according to Claim 1 and those of D1 and D2, a formal overlapping part exists. D1 and D2 disclose, however, a different activity, i.e. the compounds are described as being CNS active or having H1 antagonistic properties. The teachings of D1 and D2 are an additional indication that the presently formulated compound claims cannot be regarded a reasonable generalisation of the tested examples. Similar and/or overlapping compounds possess a completely different pharmacological profile.

#### 4. INDUSTRIAL APPLICABILITY

For the assessment of the presently worded Claims 18-40 on the question whether their subject-matter is industrially applicable, no unified criteria exist in the PCT. The patentability under national patent laws can also be dependent on the formulation of the claims. The EPO, for example, does not recognize the subject-matter of claims to the use of a compound in medical treatment as being industrially applicable, but will allow, however, claims to a known compound for first medical use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

### SECTION VIII

Due to the lack of conciseness, at least the process claims 14-16 do not fulfil the requirements of Art. 6 PCT.

# PATENT COOPERATION TREATY

## PCT

### INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 71 125 a/se	<b>FOR FURTHER ACTION</b>		See Notification of Transmittal of International Preliminary Examination Report (PCT/IPEA/416)
International application No. PCT/EP97/03245	International filing date (day/month/year) 20/06/1997	Priority date (day/month/year) 20/06/1996	
International Patent Classification (IPC) or national classification and IPC C07D401/12			
Applicant KLINGE PHARMA GMBH et al.			

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.



2. This REPORT consists of a total of **5** sheets, including this cover sheet.

- ☒ This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

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- II ☐ Priority
- III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
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Date of submission of the demand 26/11/1997	Date of completion of this report 05. 10. 98
Name and mailing address of the IPEA/   European Patent Office D-80298 Munich Tel. (+49-89) 2399-0, Tx: 523656 epmu d Fax: (+49-89) 2399-4465	Authorized officer  Von Daacke, A  Telephone No. (+49-89) 2399-8286 

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP97/03245

## I. Basis of the report

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

### Description, pages:

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### Claims, No.:

1-40 as originally filed

41 as received on 31/07/1998 with letter of 31/07/1998

2. The amendments have resulted in the cancellation of:

- ☐ the description, pages:  
☐ the claims, Nos.:  
☐ the drawings, sheets:

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

## V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

### 1. Statement

Novelty (N)	Yes: Claims 1-41
	No: Claims
Inventive step (IS)	Yes: Claims 6-13,41
	No: Claims 1-5,14-40
Industrial applicability (IA)	Yes: Claims 1-41
	No: Claims

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/EP97/03245

---

**2. Citations and explanations**

**see separate sheet**

**VIII. Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

**see separate sheet**

## SECTION V

### 1. PRIOR ART

The documents cited in the International Search Report

D1 = EP-A-0 330 026

D2 = EP-A-0 343 307

*3 in claim type et. 26*  
have been considered for the examination procedure.

### 2. NOVELTY

The claimed subject-matter is considered to be novel. Compound 3 of D1 is excluded via a disclaimer at the end of Claim 1. D2 compounds do not include an alkenylene spacer 'A'. The D1 and D2 compounds are described as having CNS or H1 antagonistic activities (Article 33(2) PCT).

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The subject-matter of Claims 1-5 and 14-40 does not fulfil the requirements of Art 33(3) PCT for the following reasons.

The application includes activity tests for seven compounds which are structurally very close together:  $R^1-R^4 = H$ ,  $k=0$ ,  $A = -CH=CH-$ ,  $D = \text{butylene}$ ,  $E = \text{piperidine-1,4-diyl}$ . Only  $G$  has different, but similar meanings. The Representative has filed additional experimental results and pharmaceutical tests which demonstrate that the structural unit D-E-G can be varied to a certain extent without any loss of the desired activity. For example, the unit 'G' may denote an aliphatic, aromatic or heteroaromatic system, wherein the aromatic ring is optionally substituted. The 'left' part of the molecule, i.e.  $R^1$ ,  $R^2$ ,  $R^3$ , and mostly  $R^4$ , as well still denote hydrogen in all of the tested compounds. Only table 1 which includes 'exemplary' compounds shows values other hydrogen for  $R^1$ . Even though it would be assumed that all of the exemplified compounds do actually exhibit the alleged activity what is not yet convincingly shown, only the object of Claims 6-13 can be regarded as inventive, i.e. solve the subjective problem for providing cytostatic and immunosuppressive agents. Any preceding claims include broad definitions

which cannot be regarded as a reasonable generalisation of the examples. In particular due to the definitions of  $R^1$ - $R^4$  and possible substitutions of aromatic systems thereof (see at the end of the respective claims).

The process Claims 14-16 include preparation steps already known such that an Inventive step cannot per se be based thereupon.

Since Claims 18-40 relate to the pharmaceutical use (different categories) all of these claims do also not satisfy Art. 33(3) PCT.

Claim 17 covering the intermediate compounds with  $G=H$  does not fulfil the requirements of Art. 33(3) EPC, as well because it is referred back to Claims 1-7.

Between the present compounds according to Claim 1 and those of D1 and D2, a formal overlapping part exists. D1 and D2 disclose, however, a different activity, i.e. the compounds are described as being CNS active or having H1 antagonistic properties. The teachings of D1 and D2 are an additional indication that the presently formulated compound claims cannot be regarded a reasonable generalisation of the tested examples. Similar and/or overlapping compounds possess a completely different pharmacological profile.

#### 4. INDUSTRIAL APPLICABILITY

For the assessment of the presently worded Claims 18-40 on the question whether their subject-matter is industrially applicable, no unified criteria exist in the PCT. The patentability under national patent laws can also be dependent on the formulation of the claims. The EPO, for example, does not recognize the subject-matter of claims to the use of a compound in medical treatment as being industrially applicable, but will allow, however, claims to a known compound for first medical use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

#### SECTION VIII

Due to the lack of conciseness, at least the process claims 14-16 do not fulfil the requirements of Art. 6 PCT.



31 July 1993

71 125 u6/ih

Neuer Patentanspruch 41

41. N-(4-diphenylmethyl-morpholin-2-ylmethyl)-3-(pyridin-3-yl)-acrylamide.

AMENDED SHEET

## PATENT COOPERATION TREATY

PCT

INFORMATION CONCERNING ELECTED  
OFFICES NOTIFIED OF THEIR ELECTION

(PCT Rule 61.3)

From the INTERNATIONAL BUREAU

To:

KOLB, Helga  
Hoffmann. Eitle  
Arabellastrasse 4  
D-81925 Munich  
ALLEMAGNE

Date of mailing (day/month/year) 24 December 1997 (24.12.97)		IMPORTANT INFORMATION	
Applicant's or agent's file reference 71 125 a/ea			
International application No. PCT/EP97/03245	International filing date (day/month/year) 20 June 1997 (20.06.97)	Priority date (day/month/year) 20 June 1996 (20.06.96)	
Applicant KLINGE PHARMA GMBH			

1. The applicant is hereby informed that the International Bureau has, according to Article 31(7), notified each of the following Offices of its election:

AP : GH,KE,LS,MW,SD,SZ,UG,ZW

EP : AT,BE,CH,DE,DK,ES,FI,FR,GB,GR,IE,IT,LU,MC,NL,PT,SE

National : AU,BG,BR,CA,CN,CZ,DE,FI,GB,IL,JP,KP,KR,MN,NO,NZ,PL,RO,RU,SE,SK,  
US,VN

2. The following Offices have waived the requirement for the notification of their election; the notification will be sent to them by the International Bureau only upon their request:

EA : AM,AZ,BY,KG,KZ,MD,RU,TJ,TM

OA : BF,BJ,CF,CG,CI,CM,GA,GN,ML,MR,NE,SN,TD,TG

National : AL,AM,AT,AZ,BA,BB,BY,CH,CU,DK,EE,ES,GE,GH,HU,IS,KE,KG,KZ,LC,LK,  
LR,LS,LT,LU,LV,MD,MG,MK,MW,MX,PT,SD,SG,SI,SL,TJ,TM,TR,TT,UA,UG,UZ,YU,ZW

3. The applicant is reminded that he must enter the "national phase" before the expiration of 30 months from the priority date before each of the Offices listed above. This must be done by paying the national fee(s) and furnishing, if prescribed, a translation of the international application (Article 39(1)(a)), as well as, where applicable, by furnishing a translation of any annexes of the international preliminary examination report (Article 36(3)(b) and Rule 74.1).

Some offices have fixed time limits expiring later than the above-mentioned time limit. For detailed information about the applicable time limits and the acts to be performed upon entry into the national phase before a particular Office, see Volume II of the PCT Applicant's Guide.

The entry into the European regional phase is postponed until 31 months from the priority date for all States designated for the purposes of obtaining a European patent including, where applicable, ES which cannot be elected since it is not bound by Chapter II.

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland  Facsimile No. (41-22) 740.14.35	Authorized officer:  J. Zahra  Telephone No. (41-22) 338.83.38
--	--

## PATENT COOPERATION TREATY

PCT

INFORMATION CONCERNING ELECTED  
OFFICES NOTIFIED OF THEIR ELECTION

(PCT Rule 61.3)

From the INTERNATIONAL BUREAU

To:

KOLB, Helga  
Hoffmann, Eitle  
Arabellastrasse 4  
D-81925 Munich  
ALLEMAGNE

Date of mailing (day/month/year) 24 December 1997 (24.12.97)		
Applicant's or agent's file reference 71 125 a/ea		IMPORTANT INFORMATION
International application No. PCT/EP97/03245	International filing date (day/month/year) 20 June 1997 (20.06.97)	
Applicant KLINGE PHARMA GMBH		Priority date (day/month/year) 20 June 1996 (20.06.96)

1. The applicant is hereby informed that the International Bureau has, according to Article 31(7), notified each of the following Offices of its election:

AP : GH, KE, LS, MW, SD, SZ, UG, ZW

EP : AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

National : AU, BG, BR, CA, CN, CZ, DE, FI, GB, IL, JP, KP, KR, MN, NO, NZ, PL, RO, RU, SE, SK,  
US, VN

2. The following Offices have waived the requirement for the notification of their election; the notification will be sent to them by the International Bureau only upon their request:

EA : AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

OA : BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

National : AL, AM, AT, AZ, BA, BB, BY, CH, CU, DK, EE, ES, GE, GH, HU, IS, KE, KG, KZ, LC, LK,  
LR, LS, LT, LU, LV, MD, MG, MK, MW, MX, PT, SD, SG, SI, SL, TJ, TM, TR, TT, UA, UG, UZ, YU, ZW

3. The applicant is reminded that he must enter the "national phase" before the expiration of 30 months from the priority date before each of the Offices listed above. This must be done by paying the national fee(s) and furnishing, if prescribed, a translation of the international application (Article 39(1)(a)), as well as, where applicable, by furnishing a translation of any annexes of the international preliminary examination report (Article 36(3)(b) and Rule 74.1).

Some offices have fixed time limits expiring later than the above-mentioned time limit. For detailed information about the applicable time limits and the acts to be performed upon entry into the national phase before a particular Office, see Volume II of the PCT Applicant's Guide.

The entry into the European regional phase is postponed until 31 months from the priority date for all States designated for the purposes of obtaining a European patent including, where applicable, ES which cannot be elected since it is not bound by Chapter II.

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. (41-22) 740.14.35	Authorized officer: J. Zahra Telephone No. (41-22) 338.83.38
--	--

## PATENT COOPERATION TREATY

PCT

## NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

United States Patent and Trademark  
Office  
(Box PCT)  
Crystal Plaza 2  
Washington, DC 20231  
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing:

24 December 1997 (24.12.97)

International application No.:

PCT/EP97/03245 ✓

Applicant's or agent's file reference:

71 125 a/ea

International filing date:

20 June 1997 (20.06.97)

Priority date:

20 June 1996 (20.06.96)

Applicant:

BIEDERMANN, Elfi et al

1. The designated Office is hereby notified of its election made:



in the demand filed with the International preliminary Examining Authority on:

26 November 1997 (26.11.97)



in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was

was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO  
34, chemin des Colombettes  
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer:

J. Zahra

Telephone No.: (41-22) 338.83.38

## PATENT COOPERATION TREATY

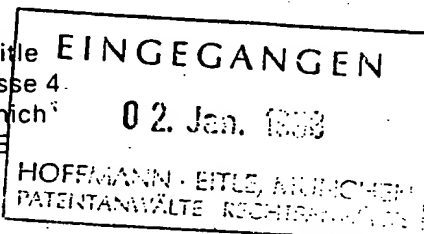
PCT

From the INTERNATIONAL BUREAU

NOTICE INFORMING THE APPLICANT OF THE  
COMMUNICATION OF THE INTERNATIONAL  
APPLICATION TO THE DESIGNATED OFFICES

(PCT Rule 47.1(c), first sentence)

To:

KOLB, Helga  
Hoffmann, Eitle  
Arabellastrasse 4  
D-81925 Munich  
ALLEMAGNE

Date of mailing (day/month/year) 24 December 1997 (24.12.97)		
Applicant's or agent's file reference 71 125 a/ea		IMPORTANT NOTICE
International application No. PCT/EP97/03245	International filing date (day/month/year) 20 June 1997 (20.06.97)	Priority date (day/month/year) 20 June 1996 (20.06.96)
Applicant KLINGE PHARMA GMBH et al		

1. Notice is hereby given that the International Bureau has communicated, as provided in Article 20, the international application to the following designated Offices on the date indicated above as the date of mailing of this Notice:  
AU, BR, CA, CN, EP, IL, JP, KP, KR, NO, PL, SK, US

In accordance with Rule 47.1(c), third sentence, those Offices will accept the present Notice as conclusive evidence that the communication of the international application has duly taken place on the date of mailing indicated above and no copy of the international application is required to be furnished by the applicant to the designated Office(s).

2. The following designated Offices have waived the requirement for such a communication at this time:  
AL, AM, AP, AT, AZ, BA, BB, BG, BY, CH, CU, CZ, DE, DK, EA, EE, ES, FI, GB, GE, GH, HU, IS, KE, KG, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NZ, OA, PT, RO, RU, SD, SE, SG, SI, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW

The communication will be made to those Offices only upon their request. Furthermore, those Offices do not require the applicant to furnish a copy of the international application (Rule 49.1(a-bis)).

3. Enclosed with this Notice is a copy of the international application as published by the International Bureau on 24 December 1997 (24.12.97) under No. WO 97/48696

## REMINDER REGARDING CHAPTER II (Article 31(2)(a) and Rule 54.2)

If the applicant wishes to postpone entry into the national phase until 30 months (or later in some Offices) from the priority date, a demand for international preliminary examination must be filed with the competent International Preliminary Examining Authority before the expiration of 19 months from the priority date.

It is the applicant's sole responsibility to monitor the 19-month time limit.

Note that only an applicant who is a national or resident of a PCT Contracting State which is bound by Chapter II has the right to file a demand for international preliminary examination.

## REMINDER REGARDING ENTRY INTO THE NATIONAL PHASE (Article 22 or 39(1))

If the applicant wishes to proceed with the international application in the national phase, he must, within 20 months or 30 months, or later in some Offices, perform the acts referred to therein before each designated or elected Office.

For further important information on the time limits and acts to be performed for entering the national phase, see the Annex to Form PCT/IB/301 (Notification of Receipt of Record Copy) and Volume II of the PCT Applicant's Guide.

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